EXTENDED REPORT

Sex: a major predictor of remission in early rheumatoid arthritis?

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Background: The treatment goal of early rheumatoid arthritis is remission. This study reports remission rates in clinical practice using a cohort of patients with early rheumatoid arthritis.

Methods: 698 patients with early rheumatoid arthritis were included. Mean age at inclusion was 58 years and mean disease duration was 6.4 months; 64% of the patients were women, 56% were positive for antibodies to cyclic citrullinated peptide and 60% were positive for rheumatoid factor. Remission was defined as a disease activity score <2.6, with or without ongoing treatment with drugs for rheumatoid arthritis.

Results: After 2 years, 261 of 689 patients were in remission (37.9%), and after 5 years, the remission rate was 38.5%. However, only 26.1% were in remission at both these time points. Multiple logistic regression analyses found sex to be a main predictor for remission. Thus, significantly fewer women were in remission after 2 years (32.1% *v* 48%, p=0.001) after 5 years (30.8% *v* 52.4%, p=0.001) and at both these time points (19.1% *v* 39.3%, p=0.001). Although disease activity was not with certainty more pronounced in women at onset of disease, the disease course became markedly worse in women. The disparity in remission frequency between women and men could not be explained by differences in disease duration, age or treatment with disease modifying antirheumatic drugs or glucocorticoids.

Conclusions: Early remission of rheumatoid arthritis by 28-joint Disease Activity Score<2.6 was as frequent or more frequent in this study than in most previous reports. Importantly, women had more severe disease with a considerably lower remission rate than men, although the disease activity before treatment seemed similar.

The present goal of treatment of early rheumatoid arthritis is remission, a state with few or no signs of ongoing disease, with or without treatment with antirheumatic drugs.

Remission is defined by varying criteria. In this study, remission was defined as <2.6 on the 28-joint Disease Activity Score (DAS28).[1 2] This criterion shows strong agreement with the criteria for remission proposed by the American Rheumatism Association (ARA),[3] and has been shown to be associated with slow radiological progression and preserved function.[4]

In previous cohort studies, depending on the study design, criteria used and treatment given, the frequency of remission in patients with early rheumatoid arthritis has ranged between 10% and 40% after a disease duration of 3–5 years.[5 6]

It has been known for a long time that women are at greater risk for severe rheumatoid arthritis than men.[7 8] For example, women with rheumatoid arthritis report more severe symptoms than men,[9] and have a more severe course of disease in terms of disease activity, functional capacity and joint destruction,[10] and a higher prevalence of work disability.[11] Despite this, earlier studies on remission rates in patients with rheumatoid arthritis have not produced separate analyses for women and men.

In this article, we report the frequency of remission in a large inception cohort of patients with rheumatoid arthritis. Among baseline demographic and clinical characteristics, we looked for major predictors of remission during a follow-up period of 5 years.

PATIENTS AND METHODS

Patients

The patients in this study are included in the ''BARFOT'' (Better Anti-Rheumatic FarmacOTherapy) project,[12] a multicentre (six rheumatological units from southern Sweden) observational study of patients with recent onset of rheumatoid arthritis (disease duration ⩽1 year) satisfying the 1987 ACR classification criteria.[13]

During the time period September 1995 to September 1999, 698 consecutive patients were included in the BARFOT programme. At follow-up after 2 years, all 698 patients were still in the study and after 5 years, 608 patients were still in the study. Thus, 90 patients were not available for follow-up after 5 years.; 18 patients had moved, 37 had died and, because of various reasons, 35 patients did not appear at follow-up.

All patients gave their informed consent and the ethical committees approved the study.

Methods

A clinical assessment was performed at inclusion into BARFOT (baseline), and thereafter at predefined intervals of 3, 6, 12, 18, 24 and 60 months. Remission was defined as a DAS28 <2.6 with or without ongoing treatment with antirheumatic drugs, in accordance with Prevoo *et al*.[2]

Remission is most often represented by a single point in time, which may limit its clinical validity. Instead, a longer time period might more adequately reflect important remission. In an attempt to accomplish this, remission was assessed not only at certain points in time but also at periods of time using the scheduled follow-up visits. Thus, point remission was assessed at 18, 24 and 60 months and period remission was defined as being in remission at ⩾2 consecutive follow-up visits—18 and 24 months, 24 and 60 months, or 18, 24 and 60 months.

Abbreviations: anti-CCP, antibodies to cyclic citrullinated peptide; ARA, American Rheumatism Association; BARFOT, Better Anti-Rheumatic FarmacOTherapy; CRP, C reactive protein; DAS28, 28-joint Disease Activity Score; DMARDs, disease-modifying antirheumatic drugs; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; SOFI, Signals Of Functional Impairment

Disease activity was assessed by the DAS, using a 28-joint count, DAS28.[1 14] At inclusion, 122 DAS values and at 2 years, four original DAS values were transformed into DAS28 by a formula described by Van Gestel *et al*.[15]

Experienced pain (pain) was assessed by a 0–100 mm Visual Analogue Scale. Morning stiffness was expressed in minutes. A 5-stage Likert scale was used for the doctor's assessment of current disease activity (doctor's assessment). Acute-phase reactions were measured by erythrocyte sedimentation rate (ESR; mm/h) and C reactive protein (CRP; mg/l), according to standard laboratory methods.

Functional impairment was measured by the Signals Of Functional Impairment (SOFI) index, a physical performance test consisting of four items for hand, three for upper limb and four for lower limb function.[16] Functional disability was assessed using the Swedish version[17] of the Stanford Health Assessment Questionnaire (HAQ).

Antibodies to cyclic citrullinated peptide (anti-CCP) were analysed using the Immunoscan rheumatoid arthritis ELISA CCP2 test (Euro-Diagnostica, Malmö, Sweden).

Rheumatoid factor was analysed using the Serodia rheumatoid arthritis agglutination test (Fujirebio, Tokyo, Japan).

Statistics

Statistical analyses were performed using SPSS V.14.0 statistical software. To test differences between groups, the Mann–Whitney U test or the independent samples t test was used for continuous variables, and the χ^2 test for proportions. For paired samples, the Wilcoxon signed-rank test was used. All significance tests were two tailed and conducted at the 0.05 significance level.

Among demographic and baseline clinical variables assessed in this study, sex, age and disease duration at inclusion, smoking status, anti-CCP, rheumatoid factor, DAS28, CRP, HAQ and SOFI have been previously reported to be related to outcome in rheumatoid arthritis.[18 19] To assess the possible association of these variables with remission, univariate analyses were performed by the independent samples t test for the continuous variables age, disease duration, baseline DAS28, HAQ and SOFI, by the Mann–Whitney U test for CRP and by the χ^2 test for the categorical variables sex, anti-CCP, rheumatoid factor and smoking. Variables showing a significance level of $p<0.1$ were included into a multiple logistic regression analysis with backward elimination. The criterion for deletion of a variable from the model was set at $p<0.05$.

RESULTS

Baseline characteristics

Table 1 shows the demographic and clinical variables at baseline. The mean age of the patients at baseline was 58 years, 64% were women and mean disease duration at inclusion was 6.2 months. Most patients had moderate or severe disease activity. Thus, only 6 (0.9%) patients had a DAS28 score below the limit for remission and 5.1% had a DAS28 value indicating low disease activity. However, according to the doctor's assessments, 23% had low disease activity. The mean (standard deviation) HAQ score indicated marked disability for many patients already in early stages of the disease. Anti-CCP was found in 56% of the patients and 60% had positive rheumatoid factor.

Table 1 Baseline characteristics of the 698 patients

	Mean (SD)	n (%)
Age (years)	58 (15)	
Sex, women		446 (64)
Disease duration (months)	6.2 (3.2)	
Smoking, previous or current		385 (55)
Anti-CCP positivity		373 (56)
RF positivity		400 (60)
Morning stiffness (min)	126 (123)	
Pain (0–100 mm VAS)	46 (24)	
Doctor's assessment		
No activity		8 (1)
Low activity		155 (23)
Moderate activity		383 (57)
High activity		118 (18)
Maximum activity		7 (1)
DAS28 (0–10)	5.27 (1.25)	
HAQ score (0–3)	1 (0.65)	
SOFI (0–44)	8 (6)	
CRP (mg/l)	20 (7/50)*	

CCP, cyclic citrullinated peptide; CRP, C reactive protein; DAS28, disease activity score using a 28-joint count; HAQ, health assessment questionnaire; RF, rheumatoid factor; SOFI, signals of functional impairment.
*Median (25/75 centiles).

Remission

After 18 months, 34.5% of the patients were in remission (remission^{18mo}). At the 24-month follow-up, 37.9% were in remission (remission^{24mo}), as were 38.5% at the 60-month follow-up (remission^{60mo}). Remission at both the 18-month and 24-month follow-ups (remission$^{18+24mo}$) was found in 162 (26.3%) patients. At the 24- and 60-month follow-ups, remission (remission$^{24+60mo}$) was noted in 26.3% of the patients. Finally, remission at all three time points (remission$^{18+24+60mo}$) was seen in 105 of 537 (19.6%) patients.

Prediction of remission

The univariate analysis showed an association ($p<0.1$) between being in remission at all point and period remissions and the following baseline variables: sex, duration of the disease at inclusion, anti-CCP, rheumatoid factor, DAS28 and HAQ. SOFI was not associated with remission^{24mo} and remission$^{24+60mo}$. Smoking was only associated with remission^{60mo} and remission$^{24+60mo}$, whereas CRP was not associated with remission at any time.

Table 2 shows the multiple logistic regression analyses for all point and period remissions. Male sex, short disease duration, low baseline DAS28, low baseline HAQ score and rheumatoid factor negativity were independently associated with remission. Thus, sex seemed to be a strong predictor of remission, but patients' age and disease duration at inclusion could be confounding factors. However, age was probably not a confounder, as this variable was associated only with sex and not with remission. In contrast, disease duration at inclusion was associated with both remission and sex. However, when sex, disease duration and their interaction term were analysed in a forward logistic regression model for all remission occasions, the odds ratios for sex were still significant, and no interaction was shown.

Thus, on the basis of the regression analyses, male sex emerged as a major independent predictor of remission. This prompted us to further analyse the relationship between sex and remission.

Overall influence of sex

For women, the frequency of remission^{18mo}, remission^{24mo} and remission^{60mo} was 30.4%, 32.1% and 30.8%, respectively, and for men, the corresponding figures were significantly higher, 41.7%, 48.0% and 52.4% ($p = 0.001$ for all three comparisons).

In women, period remission was infrequent. Thus, remission$^{18+24mo}$, remission$^{24+60mo}$ and remission$^{18+24+60mo}$, were only 22.1%, 19.1% and 13.8%, respectively. In men, these figures were significantly higher, 33.8 ($p = 0.002$), 39.3 ($p = 0.001$) and 30.3% ($p = 0.001$), respectively.

To investigate whether the sex difference in remission rate would also be evident in the presence of more stringent criteria, the clinical criteria described by Mäkinen *et al*[20] were applied. The criteria are as follows: no swollen joints, no tender joints and normal ESR (<30 mm in women and <20 mm in men). By these criteria, remission^{24mo} was achieved by 17.8% of the women and 26.8% of the men (p = 0.005), remission^{60mo} by 21% of the women and 28.5% of the men (p = 0.039) and remission$^{24+60mo}$ by 9.5% of women and 16.4% of men (p = 0.013).

Thus, by these stringent remission criteria, overall remission rates were considerably lower than those by the DAS28 criterion, but the significant sex difference remained.

Influence of age at onset of disease

The mean (SD) age at onset of rheumatoid arthritis was 58 (15) and 55 (16) years for women and 61 (14) for men, p = 0.001.

The patients were divided into two groups, above and below the mean age at onset of disease for women and men.

No significant differences in remission rates were noted between younger versus older women or men. Thus, for example, at the 24-month follow-up, 34.9% of the women in the younger age group were in remission versus 30% in the older age group, p = 0.27. The figures for men were 50% versus 45.4%, respectively, p = 0.47.

Influence of disease activity and function at baseline

Table 3 shows the clinical variables at inclusion into BARFOT, split by sex. Women had significantly higher baseline DAS28 and pain scores, whereas CRP was higher in men. No significant differences were observed between women and men with regard to morning stiffness or the doctor's assessment of current disease activity. With regard to function in activities of daily living, women had significantly higher HAQ score at inclusion, whereas the SOFI physical performance score disclosed no significant sex difference.

Anti-CCP was positive in 55.9% of women and in 56.2% of men, while rheumatoid factor was detected in 59.1% of woman and 61.6% of men(p = 0.52 and 0.94, respectively).

Thus, despite a higher baseline DAS28, the overall data do not indicate with certainty that women had more severe rheumatoid arthritis than men already at inclusion into the study.

Disease activity and function during follow-up

At the 2-year follow-up (table 4), DAS28 had decreased significantly compared with baseline in both sex groups (mean (SD) change −2.09 (1.62), p = 0.001) but significantly less in women than in men (mean (SD) change −1.96 (1.58) *v* −2.32 (1.58), p = 0.001). At the 5-year follow-up (table 5), mean (SD) DAS28 had decreased by −2.07 (1.67) p = 0.001), and again significantly less in women (−1.92 (1.67)) than in men (−2.32 (1.64)), p = 0.001. Furthermore, the doctor's assessment indicated that women had significantly higher disease activity both after 2 years and after 5 years. Pain was also more pronounced in women at these follow-ups. Morning stiffness was significantly more pronounced in women after 2 years, but not after 5 years. The level of CRP, which was higher in men at

Table 2 Prediction of remission; final steps in multiple logistic regression analyses with backward elimination

	Baseline variable	OR	95% CI		p Value
Remission^{18mo}	Male sex	1.557	1.062	2.283	0.023
	Disease duration	0.908	0.854	0.966	0.002
	RF positivity	0.516	0.355	0.749	0.001
	DAS28	0.777	0.659	0.915	0.002
	HAQ	0.698	0.505	0.967	0.031
	Constant	4.057			0.018
Remission^{24mo}	Male sex	1.713	1.208	2.431	0.003
	Disease duration	0.908	0.859	0.960	0.001
	CCP positivity	0.630	0.448	0.886	0.008
	DAS28	0.809	0.695	0.942	0.006
	HAQ	0.644	0.478	0.869	0.004
	Constant	3.362			0.025
Remission^{60mo}	Male sex	2.837	1.905	4.224	0.001
	Disease duration	0.925	0.870	0.983	0.012
	RF positivity	0.556	0.379	0.815	0.003
	DAS28	0.667	0.568	0.785	0.001
	Current or previous smoker	0.668	0.453	0.985	0.042
	Constant	3.637			0.029
Remission$^{18+24mo}$	Male sex	1.530	1.022	2.292	0.039
	Disease duration	0.907	0.848	0.969	0.004
	RF positivity	0.578	0.389	0.859	0.007
	DAS28	0.767	0.645	0.913	0.003
	HAQ	0.561	0.393	0.801	0.001
	Constant	3.611			0.041
Remission$^{24+60mo}$	Male sex	2.873	1.871	4.411	0.001
	Disease duration	0.871	0.812	0.935	0.001
	RF positivity	0.519	0.342	0.788	0.002
	DAS28	0.750	0.625	0.900	0.002
	HAQ	0.640	0.438	0.937	0.022
	Current or previous smoker	0.623	0.408	0.951	0.028
	Constant	2.428			0.16
Remission$^{18+24+60mo}$	Male sex	2.641	1.632	4.273	0.001
	Disease duration	0.883	0.812	0.959	0.003
	RF positivity	0.470	0.291	0.759	0.002
	DAS28	0.750	0.612	0.918	0.005
	HAQ	0.563	0.360	0.881	0.012
	Constant	1.564			0.54

CCP, cyclic citrullinated peptide; DAS28, disease activity score using a 28-joint count; HAQ, Health Assessment Questionnaire; RF, rheumatoid factor.

Table 3 Sex differences as to clinical variables at baseline

	Women (n = 446)	Men (n = 252)	Difference	
	Mean (SD) n (%)	Mean (SD)	n (%)	p Value
Morning stiffness	128 (111)	121 (143)		0.43
Pain	47 (24)	43 (23)		0.027
	No activity	3 (1)	5 (2)	
	Low activity	96 (22)	59 (24)	
Doctor's assessment	Moderate activity	250 (59)	133 (55)	0.5
	High activity	73 (17)	45 (18)	
	Maximum activity	5 (1)	2 (1)	
DAS28	5.37 (1.20)	5.09 (1.33)		0.005
HAQ score	1.11 (0.66)	0.83 (0.59)		0.001
SOFI	8 (6)	9 (6)		0.11
CRP	18 (6–42)*	27 (10–54)*		0.001

CRP, C reactive protein; DAS28, disease activity score using a 28-joint count; HAQ, Health Assessment Questionnaire; SOFI, Signals Of Functional Impairment.
*Median (25th–75th centile).

baseline, became similar after a follow-up of 2 years and 5 years (tables 4, 5).

During follow-up, HAQ score and SOFI improved significantly in both women and men (data not shown in detail). However, the 2-year and 5-year mean HAQ scores, disclosing difficulties concerning activities of daily living, were significantly higher in women, $p = 0.001$, at both time points. By contrast, the mean SOFI score was similar in the two groups at the 2-year and 5-year follow-ups.

Consequently, the disease course during these 5 years of follow-up seemed considerably worse for women than for men.

Treatment with anti-rheumatic drugs

In the BARFOT programme, the treating rheumatologists are actively encouraged to try to hold the inflammatory process back as much as possible with the motto ''as few days with active inflammation as possible''. The attainment of this goal is ''no activity'' on the Likert scale for the doctor's assessment of current disease activity.

Treatment with disease modifying antirheumatic drugs (DMARDs) was studied at baseline and at the 2-year and 5-year follow-ups (table 6). The DMARDs used were divided into five groups:

1. Methotrexate
2. Sulphasalazine
3. Other DMARD monotherapy
4. DMARD combination therapy
5. Biological drugs.

Women and men were comparable both as regards the proportion of patients treated with DMARDs and the kind of DMARD given. At baseline, more than >80% recieved DMARD monotherapy, usually sulphasalazine or methotrexate.

About 55% of the women and 57% of the men were included into the study within 1–6 months ($p = 0.61$) of onset of rheumatoid arthritis. Hence, DMARD treatment was initiated at a similar time point in the disease course in women and men.

About 30% of the patients (both women and men) were off treatment with DMARDs after 2 years and some more after 5 years. A major reason for the cessation of treatment may be that in this population-based study, several patients benefited from a benign disease course and were judged to have low disease activity by the treating doctor.

Treatment with glucocorticoids

At baseline, 42% of the women and 41% of the men were given prednisolone. At 2 years, 35% of the women and 33% of the men were still treated with prednisolone, and after 5 years, 23% of the women and 17% of the men were receiving that treatment.

At baseline, women treated with prednisolone had a mean daily dose of 7.8 mg, whereas men received a mean daily dose of 8.1 mg prednisolone, $p = 0.30$. After 2 and 5 years, the corresponding figures for women and men were 6.2 mg *v* 6.5 mg daily ($p = 0.33$) and 4.9 mg *v* 5.1 mg daily ($p = 0.77$), respectively.

Thus, the data indicate that glucocorticoid treatment was the same in both women and men, with regard to both number of patients treated and the daily prednisolone dose.

Table 4 Sex differences with regard to to clinical variables at the 2-year follow-up

	Women (n = 446)		Men (n = 252)		Difference
	Mean (SD)	n (%)	Mean (SD)	n (%)	p Value
Morning stiffness	59 (84)		45 (67)		0.021
Pain	30 (26)		25 (23)		0.003
	No activity	123 (28)		104 (42)	
	Low activity	224 (51)		117 (47)	
Doctor's assessment	Moderate activity	84 (19)		22 (9)	0.001
	High activity	6 (1)		5 (2)	
	Maximum activity	0 (0)		0 (0)	
DAS28	3.41 (1.39)		2.81 (1.33)		0.001
HAQ score	0.69 (0.68)		0.47 (0.53)		0.001
SOFI	6 (5)		6 (6)		0.10
CRP	9 (4–13)*		9 (4–14)*		0.22

CRP, C reactive protein; DAS28, disease activity score using a 28-joint count; HAQ, Health Assessment Questionnaire; SOFI, Signals Of Functional Impairment.
*Median (25th–75th centile).

Table 5 Sex differences with regard to clinical variables at the 5-year follow-up

	Women (n = 393)		Men (n = 215)		Difference
	Mean	n (%)	Mean	n (%)	p Value
Morning stiffness	50 (63)		44 (67)		0.31
Pain	32 (27)		26 (24)		0.004
	No activity	125 (32)		101 (48)	
	Low activity	189 (49)		85 (40)	
Doctor's assessment	Moderate activity	65 (17)		20 (9)	0.001
	High activity	9 (2)		6 (3)	
/p>	Maximum activity	0 (0)		0 (0)	
DAS28	3.45 (1.42)		2.83 (1.37)		0.0005
HAQ score	0.76 (0.68)		0.54 (0.58)		0.0005
SOFI	7 (6)		7 (6)		0.62
CRP	9 (4–13)*		9 (7–13)*		0.17

CRP, C reactive protein; DAS28, disease activity score using a 28-joint count; HAQ, Health Assessment Questionnaire; SOFI, Signals Of Functional Impairment.
*Median (25th–75th centile).

DISCUSSION

The DAS28 remission criterion used in this study was presented in 1996,[2] and found to conform well to the preliminary ARA criteria from 1981.[3] These results were confirmed by Balsa *et al*,[5] who found that the DAS28 remission criterion reflected the ARA criteria well, with a specificity of 82% and a sensitivity of 81% in a study on 788 patients with rheumatoid arthritis. Likewise, Fransen *et al*[21] found, in a study on 378 patients with early rheumatoid arthritis, that DAS28 <2.6 corresponds to fulfilment of the ARA criteria for clinical remission in rheumatoid arthritis almost as well as the original DAS criterion for remission (DAS <1.6). However, Mäkinen *et al*,[22] in a recent study on 196 patients with rheumatoid arthritis, emphasise that although the DAS28 criterion reflects ARA clinical remission, several patients being in DAS28 remission still have tender or swollen joints, indicating some ongoing disease activity.

Landewé *et al*[23] recently reported that the remission criterion based on the original DAS is more conservative than that based on the DAS28, and recommended cautious use of rating remission by DAS28. Among patients discordant for remission by DAS and DAS28, most of their patients were in remission by DAS28, but not by DAS, owing to the presence of swollen or tender joints in the lower extremity not assessed in the 28-joint index used in DAS28. However, in this study, this tendency was not seen in patients having values for both DAS and DAS28.

This study on patients in clinical practice has shown that almost 40% of patients with early rheumatoid arthritis were in remission after a follow-up time of 2 or 5 years. This figure is as high or higher than those previously reported in similar studies[12 24–27] where DAS28 <2.6 has been used as the criterion of remission. The frequency of remission observed in this study is also similar to those reported from recent clinical trials of antirheumatic drugs.[28–31] Thus, in most studies, most patients were not in remission after 2 or 5 years, and accordingly not optimally treated. However, substantial increases in remission rates using standardised monitoring of patients at regular visits instead of ordinary clinical assessment by rheumatologists has recently been reported. Thus, Grigor *et al*[32] introduced an 18-month programme with monthly follow-up visits allowing

Table 6 Disease-modifying antirheumatic drug treatments at baseline and after 24 and 60 months

	Women		Men		Difference
	n	%	n	%	p Value
DMARDs at baseline					0.93
No DMARD	66	15	41	16	
MTX	174	39	92	37	
SAL	150	34	86	34	
Other DMARD Monotherapy	54	12	31	12	
DMARD Combination	2	0	2	1	
Biologicals	0	0	0	0	
DMARDs at 24 months					0.74
No DMARD	119	27	77	31	
MTX	173	39	94	37	
SAL	56	13	35	14	
Other DMARD Monotherapy	49	11	21	8	
DMARD Combination	41	9	22	9	
Biologicals	6	1	2	1	
DMARDs at 60 months					0.34
No DMARD	141	36	69	32	
MTX	132	34	77	36	
SAL	24	6	20	9	
Other DMARD Monotherapy	36	9	22	10	
DMARD Combination	41	10	14	7	
Biologicals	19	5	13	6	

Biological, biological drugs; DMARD, disease-modifying antirheumatic drug; MTX, methotrexate; SAL, sulphasalazine.

treatment decisions to be made from the current DAS value. This method resulted in a point remission rate by DAS <1.6 as high as 65%. Moreover, Mäkinen *et al,*[20] using more stringent criteria admitting no swollen or tender joints and no increase in ESR, obtained virtually the same overall remission rates as those in this study. This may be due to the fact that almost all their study patients were receiving DMARD treatment for almost the entire 5-year follow-up time.

Most studies use point remission—that is, the rating of remission at a certain point in time during the disease course—regardless of ongoing drug treatment. However, the ARA clinical remission criteria demand that the remission criteria are fulfilled for 2 successive months, whereas the DAS and DAS28 remission criteria do not include time periods. This may be a shortcoming, as remission based on a DAS or DAS28 at a single time point might be due to temporary fluctuations in disease activity. As sustained remission should be the ultimate goal of treatment, the remission criteria used should be fulfilled during long-term defined intervals. In this study, in clinical practice, the DAS28 remission criterion was assessed only at the scheduled follow-up visits. Patients in remission on two or three consecutive follow-up visits during a period from 18 to 60 months after start of treatment were considered as being in period remission. As expected, and also shown by others having used a similar approach,[20 33] the rates of period remission were considerably lower than those of point remission, confirming the suspicion that remission defined at a single point in time may overestimate outcome. However, to show that patients benefit from true sustained remission, this state should be more precisely characterised and preferably include more frequent assessments. An attempt to achieve this has recently been made within the frame of the TEMPO study,[30] where sustained remission was assessed by analyses of DAS or DAS28 scores every fourth week during a 6-month period. However, further work is needed before we know which optimum time period spent in remission is clinically relevant.[30]

In the multiple logistic analyses in this study, male sex seemed to be an independent predictor of being in remission both at 2 and 5 years. As mentioned in the introduction, in earlier studies on patients with established rheumatoid arthritis, female sex was found to be associated with poor outcome. This is also in agreement with a limited number of studies on patients with early rheumatoid arthritis. Möttönen *et al*[34] found, in an observational study on patients with early rheumatoid arthritis, that remission by the ARA criteria was significantly less frequent in women, although both sexes had been treated similarly. Likewise, Tengstrand *et al*[35] found DAS28 and Kuiper *et al*[10] found DAS to be higher in women (postmenopausal women in the Kuiper *et al* study) than in men at follow-up. However, in the Tengstrand *et al* study but not in Kuiper *et al's* study, this difference was already present at the start of the study, before antirheumatic treatment had been introduced. In this study, baseline DAS28 was significantly higher in women, but when the other variables reflecting disease activity and function were weighed together, it could not be stated with certainty that women had a more active disease at inclusion—that is, within 1 year of the initial indication of rheumatoid arthritis. Nevertheless, after 2 and 5 years of follow-up, most variables reflecting disease activity clearly indicated that women had a more severe clinical course of disease than men.

The reasons for the difference in remission rates between sexes in our study are unclear. Age did not seem to play a part. Women were significantly younger than men, but younger women had the same remission rate as older women. Women were included during the first 6 months of their disease as often as were men, and treatment was most often started at the time of inclusion. Accordingly, DMARDs were given in the same way to women and men, and the mean prednisolone dose was not significantly different. Hence, treatment was not found to be delayed or of inferior quality in women.

To conclude, the remission rates in this study on early rheumatoid arthritis were as high or higher than those in most previous reports. Importantly, women had a much lower remission rate than men, although their disease activity before treatment seemed similar. The reasons for this discrepancy are presently unclear and merit further investigation. However, the data seem solid enough to call for reinforced vigilance in the frequency and quality of follow-up to achieve optimum suppression of the inflammatory process of all patients, regardless of sex.

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